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# Comparative Epidemiology of Vancomycin-Resistant Enterococci Colonization in an Acute-Care Hospital and Its Affiliated Intermediate- and Long-Term Care Facilities in Singapore

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**ABSTRACT** Vancomycin-resistant enterococci (VRE) are an important cause of nosocomial infections in acute-care hospitals (ACHs), intermediate-care facilities (ITCFs), and long-term care facilities (LTCFs). This study contemporaneously compared the epidemiology and risk factors for VRE colonization in different care settings in a health care network. We conducted a serial cross-sectional study in a 1,700-bed ACH and its six closely affiliated ITCFs and LTCFs in June and July of 2014 to 2016. Rectal swab or stool specimens were cultured for VRE. Multivariable logistic regression was used to assess for independent risk factors associated with VRE colonization. Of 5,357 participants, 523 (9.8%) were VRE colonized. VRE prevalence was higher in ACHs (14.2%) than in ITCFs (7.6%) and LTCFs (0.8%). Common risk factors between ACHs and ITCFs included prior VRE carriage, a longer duration of antibiotic therapy, surgery in the preceding 90 days, and the presence of a skin ulcer. Independent risk factors specific to ACH-admitted patients were prior methicillin-resistant *Staphylococcus aureus* carriage, a higher number of beds per room, prior proton pump inhibitor use, and a length of stay of >14 days. For ITCFs, a length of stay of >14 days was inversely associated with VRE colonization. Similarities and differences in risk factors for VRE colonization were observed between health care settings. VRE prevention efforts should target the respective high-risk patients.

**KEYWORDS** epidemiology, vancomycin-resistant enterococci, acute-care hospital, intermediate-care facilities, long-term care facilities

Vancomycin-resistant enterococci (VRE) are Gram-positive cocci with phenotypic resistance against glycopeptides (1). VRE have the ability to avoid the damage caused by ethanol-based disinfectants (2) and can survive in health care environments for prolonged periods (3), posing significant threats to patient safety. Furthermore, VRE are capable of donating resistance plasmids to methicillin-resistant *Staphylococcus aureus* (MRSA), producing vancomycin-resistant *Staphylococcus aureus* (VRSA) (4).

VRE were first reported in 1986 in acute-care hospitals (ACHs) in the United Kingdom (5). Since then, the global prevalence of VRE has risen steadily (6). *Enterococcus* is the third most prevalent nosocomial pathogen causing bacteremia (7), with 60% of *Enterococcus faecium* isolates demonstrating vancomycin resistance (8). Since the first reported case of VRE in Singapore in 1996 (9), several outbreaks of VRE have occurred (10). The first outbreak was reported in the country's largest ACH. Subsequent out-

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breaks involved multiple hospitals (11, 12), following which a rapid increase in VRE prevalence was observed in ACHs (13), raising concerns of VRE transmission to intermediate- and long-term care facilities (ILTCFs) (14).

VRE colonization is associated with increased mortality (15), particularly in leukemic, transplant, and critically ill patients, leading to early mortality (16, 17). A prolonged duration of VRE colonization after hospital discharge is associated with surgery, antibiotic use during admission, and discharge to a nursing home (18). With the frequent movement of patients between health care facilities, acute-care hospitals (ACHs) and ILTCFs form a contiguous epidemiological network (19).

Globally, the factors leading to colonization in ILTCFs are not well understood, although risk factors in ACHs have been more widely studied (20–22). A recent study in six short-stay nursing facilities in the United States which provide post-acute care to patients discharged from ACHs attempted to compare risk factors for VRE colonization on admission and at discharge from such intermediate-care facilities (ITCFs) (23). Another study in northern Italy performed point prevalence surveys in three long-term care facilities (LTCFs) to assess the prevalence and risk factors of VRE colonization (24). Thus far, the only published study that has compared the epidemiology of VRE colonization in an ACH with that in its affiliated long-term care unit was in the United States in 1997 (25). Since then, the epidemiology of VRE has changed significantly (26). To our knowledge, there have not been any recent published studies comparing the epidemiology of VRE between an ACH and its affiliated ILTCFs.

The infrastructure, clinical practice, and patient profiles in ACHs and ILTCFs differ substantially. While the general principles of infection control are applicable, interventions must be tailored to the specific context of the health care settings in order for them to be effective (14). Understanding the comparative epidemiology of VRE colonization in an interconnected health care network of an ACH, ITCFs, and LTCFs would enable the development of strategies for the prevention and control of VRE not only within institutions but also between institutions (27).

Hence, our study's objectives were to contemporaneously compare the epidemiology of VRE colonization in an ACH and its affiliated ITCFs and LTCFs in a health care network and to identify setting-specific risk factors that can guide the development of tailored infection prevention and control strategies.

## RESULTS

During the study period, 2,956, 1,244, and 1,157 patients from the ACH, ITCFs, and LTCFs, respectively, were screened for VRE. Table 1 summarizes the patients' characteristics. Participants were predominantly male ($n = 2,876$; 53.7%), and the median age was 73 years (interquartile range [IQR], 62 to 81 years). Of the 5,357 participants, 523 (9.8%) were colonized with VRE, the majority of which were genotypically *vanA* (93.3%). The VRE prevalence was higher in the ACH ($n = 419$; 14.2%) than in the ITCFs ($n = 95$; 7.6%) and LTCFs ($n = 9$; 0.8%) (Table 1). In the ACH, the VRE prevalence decreased from 19.8% in 2014 to 14.0% in 2015 to 8.9% in 2016 ($P$ value for trend [$P_{trend}$] $< 0.001$). This was consistent with the decline in the hospital's annual VRE screening colonization and clinical infection rates over the 3 years. Conversely, the VRE prevalence in LTCFs increased marginally from 0.3% in 2014 to 1.1% in 2016 ($P_{trend} = 0.12$). In ITCFs, the VRE prevalence rose from 5.1% in 2014 to 9.9% in 2015 ($P < 0.01$) and then decreased to 7.4% in 2016 ($P = 0.18$) (Fig. 1). There was no VRE outbreak in the institutions during the study period.

Regardless of the type of admitting health care facility, associations were observed between VRE colonization and the use of indwelling invasive devices, including peripheral lines and indwelling urinary catheters; exposures to proton pump inhibitors (PPI) and major classes of antibiotics, such as aminoglycosides, cephalosporins, fluoroquinolones, penicillin, and vancomycin; the presence of a wound or a skin ulcer; and prior carriage of MRSA (Table 2). Colonization with VRE was found to be associated with (i) prior surgery, prior VRE carriage, and a longer duration of antibiotic therapy in ACH and ITCF patients and (ii) the use of a percutaneous endoscopic gastrostomy tube and

**TABLE 1** Characteristics of patients and health care facilities[a]

| Characteristic | Values for patients in: | | | |
|---|---|---|---|---|
| | Total ($n$ = 5,357) | ACH ($n$ = 2,956) | ITCFs ($n$ = 1,244) | LTCFs ($n$ = 1,157) |
| Age (yr) | | | | |
| Median (IQR) | 73 (62–81) | 74 (62–82) | 73 (63–80) | 72 (61–82) |
| Range | 21–106 | 21–106 | 25–99 | 27–106 |
| No. (%) of patients >65 yr of age | 3,607 (67.3) | 1,989 (67.3) | 865 (69.5) | 753 (65.1) |
| No. (%) of patients by gender | | | | |
| Male | 2,876 (53.7) | 1,626 (55.0) | 638 (51.3) | 612 (52.9) |
| Female | 2,481 (46.3) | 1,330 (45.0) | 606 (48.7) | 545 (47.1) |
| No. (%) of patients by ethnicity | | | | |
| Chinese | 4,096 (76.5) | 2,341 (79.2) | 1,011 (81.3) | 744 (64.3) |
| Malay | 713 (13.3) | 276 (9.3) | 120 (9.6) | 317 (27.4) |
| Indian | 412 (7.7) | 254 (8.6) | 85 (6.8) | 73 (6.3) |
| Others | 136 (2.5) | 85 (2.9) | 28 (2.3) | 23 (2.0) |
| No. (%) of subsidized patients | 4,995 (93.2) | 2,709 (91.6) | 1,130 (90.8) | 1,156 (99.9) |
| No. (%) of patients with the following no. of beds per room: | | | | |
| 1 | 446 (8.3) | 422 (14.3) | 20 (1.6) | 4 (0.3) |
| 2–4 | 392 (7.3) | 283 (9.6) | 70 (5.6) | 39 (3.4) |
| 5–8 | 3,340 (62.4) | 2,067 (69.9) | 840 (67.5) | 433 (37.4) |
| >8 | 1,179 (22.0) | 184 (6.2) | 314 (25.2) | 681 (58.9) |
| No. (%) of patients screened for VRE in the following yr: | | | | |
| 2014 | 1,673 (31.2) | 976 (33.0) | 354 (28.4) | 343 (29.6) |
| 2015 | 1,794 (33.5) | 969 (32.8) | 456 (36.7) | 369 (31.9) |
| 2016 | 1,890 (35.3) | 1,011 (34.2) | 434 (34.9) | 445 (38.5) |
| No. (%) of patients with the following source of specimen: | | | | |
| Rectal swab | 5,163 (96.4) | 2,829 (95.7) | 1,210 (97.3) | 1,124 (97.2) |
| Stool | 194 (3.6) | 127 (4.3) | 34 (2.7) | 33 (2.8) |
| No. (%) of patients colonized with VRE | 523 (9.8) | 419 (14.2) | 95 (7.6) | 9 (0.8) |
| No. (%) of patients with VRE of the following genotype: | | | | |
| *vanA* | 488 (93.3) | 390 (93.1) | 90 (94.7) | 8 (88.9) |
| *vanB* | 31 (5.9) | 28 (6.7) | 2 (2.1) | 1 (11.1) |
| *vanA* and *vanB* | 4 (0.8) | 1 (0.2) | 3 (3.2) | 0 (0.0) |

[a]Abbreviations: ACH, acute-care hospital; ITCFs, intermediate-term care facilities; IQR, interquartile range; LTCFs, long-term care facilities; VRE, vancomycin-resistant enterococci.

prior hospital admission for acute care in ACH and LTCF patients. We observed that an age of >65 years, a Charlson's comorbidity index (CCI) of >5, and a longer length of stay were associated with VRE colonization in ACH patients, whereas males were more likely than females to be colonized with VRE in ITCFs.

**Multivariable analysis.** After adjusting for age, gender, comorbidities, year of screening, and the health care facility, prior VRE (odds ratio [OR], 5.23; 95% confidence interval [CI], 3.43 to 7.97; $P < 0.001$) and MRSA (OR, 1.83; 95% CI, 1.46 to 2.29; $P < 0.001$) carriage, a length of stay of >14 days (OR, 0.61; 95% CI, 0.38 to 0.96; $P = 0.03$), a higher number of beds per room (2 to 4 beds/room [OR, 1.37; 95% CI, 0.86 to 2.20; $P = 0.19$], 5 to 8 beds/room [OR, 1.61; 95% CI, 1.14 to 2.27; $P < 0.01$], and >8 beds/room [OR, 2.06; 95% CI, 1.32 to 3.23; $P < 0.01$]), exposures to PPI (OR, 1.63; 95% CI, 1.24 to 2.14; $P < 0.01$), a longer duration of antibiotic therapy (1 to 3 days [OR, 2.79; 95% CI, 1.37 to 5.70; $P < 0.01$], 4 to 7 days [OR, 3.59; 95% CI, 1.93 to 6.67; $P < 0.001$], and >7 days [OR, 5.62; 95% CI, 3.20 to 9.87; $P < 0.001$]), surgery in the past 90 days (OR, 1.44; 95% CI, 1.17 to 1.79; $P < 0.01$), the presence of a skin ulcer (OR, 1.74; 95% CI, 1.40 to 2.17; $P < 0.001$), and the use of an indwelling urinary catheter (OR, 1.63; 95% CI, 1.04 to 2.56; $P = 0.03$) were independently associated with VRE colonization (Table 3). A significant interaction between the admitting health care facility and a length of stay of >14 days was observed (OR, 2.61; 95% CI, 1.55 to 4.39; $P < 0.001$) (Table 3).

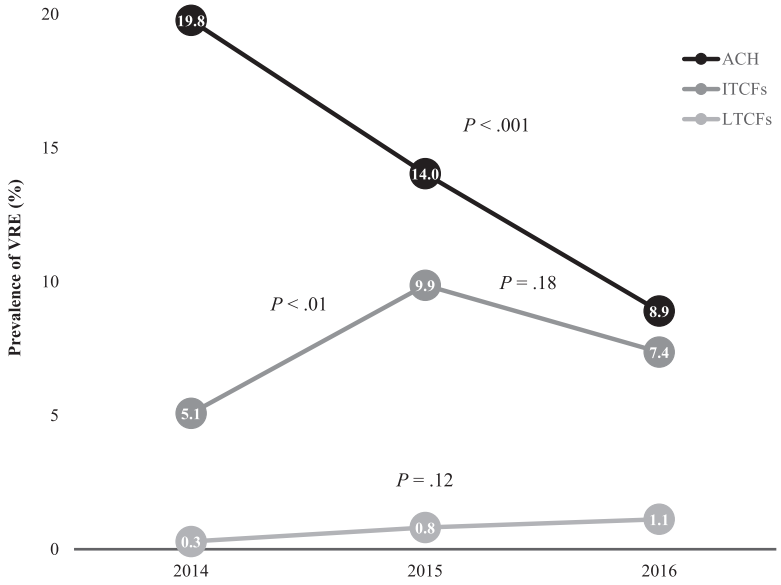


**FIG 1** Trends of vancomycin-resistant enterococci (VRE) point prevalence in the acute-care hospital (ACH), intermediate-term care facilities (ITCFs), and long-term-care facilities (LTCFs) from 2014 to 2016. *P* values were derived from the Z test.

The modifying effects of the health care facility were further assessed by stratification (Table 4). Due to the small number of VRE-colonized patients ($n = 9$) among residents of LTCFs, no significant risk factors could be identified (data not presented). As such, the stratified analysis included only the ACH and ITCFs.

For ACH-admitted patients, prior VRE (OR, 6.29; 95% CI, 3.86 to 10.25, $P < 0.001$) and MRSA (OR, 1.87; 95% CI, 1.44 to 2.43; $P < 0.001$) carriages, a length of stay of >14 days (OR, 1.71; 95% CI, 1.32 to 2.21; $P < 0.001$), a higher number of beds per room (2 to 4 beds per room [OR, 1.54; 95% CI, 0.94 to 2.53; $P = 0.09$], 5 to 8 beds per room [OR, 1.79; 95% CI, 1.24 to 2.57; $P < 0.01$], and >8 beds per room [OR, 2.12; 95% CI, 1.24 to 3.62; $P < 0.01$]), exposures to PPI (OR, 1.61; 95% CI, 1.16 to 2.22; $P < 0.01$), and a longer duration of antibiotic therapy (1 to 3 days [OR, 2.93; 95% CI, 1.34 to 6.41; $P < 0.01$], 4 to 7 days [OR, 3.35; 95% CI, 1.67 to 6.71; $P < 0.01$], and >7 days [OR, 4.44; 95% CI, 2.32 to 8.51; $P < 0.001$]), surgery in the past 90 days (OR, 1.45; 95% CI, 1.14 to 1.85; $P < 0.01$), and the presence of a skin ulcer (OR, 1.65; 95% CI, 1.27 to 2.13; $P < 0.001$) were independently associated with VRE colonization, after adjusting for potential confounders (Table 4).

For ITCFs, the significant independent factors associated with VRE colonization included prior VRE carriage (OR, 3.45; 95% CI, 1.16 to 10.28; $P = 0.03$), a length of stay of >14 days (OR, 0.51; 95% CI, 0.32 to 0.84; $P < 0.01$), >7 days of antibiotic therapy (OR, 7.80; 95% CI, 2.35 to 25.87; $P < 0.01$), surgery in the past 90 days (OR, 1.62; 95% CI, 1.00 to 2.62; $P = 0.05$), and the presence of a skin ulcer (OR, 1.99; 95% CI, 1.22 to 3.24; $P < 0.01$). No significant associations were found for a higher number of beds per room and prior admission to ACHs (the ACH in the health care network and other ACHs) (Table 4).

## DISCUSSION

This study enabled the comparison of VRE epidemiology in an ACH and its closely affiliated ILTCFs in a health care network over 3 years. VRE colonization was more prevalent in the ACH (14.2%) than in the ILTCFs, with a significantly higher prevalence in ITCFs (7.6%) than in LTCFs (0.8%). The VRE prevalence in the ACH, ITCFs, and LTCFs was lower than that reported in similar facilities in the United States (23, 28), but the low prevalence in LTCFs was similarly observed in LTCFs in two Italian cities (24).

The contemporaneous assessment identified similarities and differences in factors associated with VRE colonization in the ACH *vis-à-vis* ITCFs. For both the ACH and ITCFs,

**TABLE 2** Univariate analysis of epidemiologic and clinical risk factors for VRE colonization in ACH, ITCFs, and LTCFs[d]

| Characteristic | Value(s) for patients in: | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ACH ($n$ = 2,956) | | | ITCFs ($n$ = 1,244) | | | LTCFs ($n$ = 1,157) | | |
| | VRE positive ($n$ = 419) | VRE negative ($n$ = 2,537) | $P_1$ | VRE positive ($n$ = 95) | VRE negative ($n$ = 1,149) | $P_2$ | VRE positive ($n$ = 9) | VRE negative ($n$ = 1,148) | $P_3$ |
| Demographics | | | | | | | | | |
| Median (IQR) age (yr) | 75 (63–83) | 73 (62–82) | 0.05[b] | 74 (64–80) | 73 (63–80) | 0.83[b] | 75 (60–76) | 72 (61–82) | 0.60[b] |
| No. (%) of patients >65 yr of age | 301 (71.8) | 1,688 (66.5) | 0.03 | 68 (71.6) | 797 (69.4) | 0.65 | 6 (66.7) | 747 (65.1) | 1.00[c] |
| No. (%) of male patients | 247 (59.0) | 1,379 (54.4) | 0.08 | 60 (63.2) | 578 (50.3) | 0.02 | 6 (66.7) | 606 (52.8) | 0.51[c] |
| Comorbidities | | | | | | | | | |
| Median (IQR) CCI | 4 (2–6) | 3 (1–6) | <0.001 | 3 (2–5) | 3 (1–4) | <0.001 | 4 (1–5) | 2 (1–4) | 0.48 |
| No. (%) of patients with CCI of >5 | 144 (34.4) | 657 (25.9) | <0.001 | 15 (15.8) | 131 (11.4) | 0.20 | 2 (22.2) | 146 (12.7) | 0.32[c] |
| No. (%) of patients with the following: | | | | | | | | | |
| Congestive cardiac failure | 94 (22.4) | 390 (15.4) | <0.001 | 16 (16.8) | 80 (7.0) | <0.01 | 1 (11.1) | 83 (7.2) | 0.49[c] |
| Chronic pulmonary disease | 56 (13.4) | 317 (12.5) | 0.62 | 14 (14.7) | 85 (7.4) | 0.01 | 2 (22.2) | 88 (7.7) | 0.15[c] |
| Peptic ulcer disease | 41 (9.8) | 178 (7.0) | 0.05 | 6 (6.3) | 50 (4.4) | 0.43[c] | 0 (0.0) | 66 (5.8) | 1.00[c] |
| Peripheral vascular disease | 81 (19.3) | 239 (9.4) | <0.001 | 81 (19.3) | 239 (9.4) | <0.001 | 17 (16.4) | 273 (11.9) | 0.17 |
| Renal disease | 175 (41.8) | 731 (28.8) | <0.001 | 35 (36.8) | 221 (19.2) | <0.001 | 2 (22.2) | 174 (15.2) | 0.63[c] |
| Hemodialysis | 50 (28.6) | 121 (16.6) | <0.001 | 13 (37.1) | 56 (25.3) | 0.14 | 0 (0.0) | 14 (8.1) | 1.00[c] |
| No. (%) of patients with the following indwelling devices: | | | | | | | | | |
| Central venous line | 72 (17.2) | 248 (9.8) | <0.001 | 12 (12.6) | 65 (5.7) | <0.01 | 0 (0.0) | 11 (1.0) | 1.00[c] |
| Arterial line | 119 (28.4) | 482 (19.0) | <0.001 | 14 (14.7) | 122 (10.6) | 0.22 | 0 (0.0) | 18 (1.6) | 1.00[c] |
| Peripheral line | 413 (98.6) | 2,353 (92.8) | <0.001 | 90 (94.7) | 975 (84.9) | <0.01 | 9 (100.0) | 439 (38.2) | <0.001[c] |
| Peripherally inserted central catheter | 45 (10.7) | 96 (3.8) | <0.001 | 18 (18.9) | 64 (5.6) | <0.001 | 0 (0.0) | 13 (1.1) | 1.00[c] |
| Dialysis line | 60 (14.3) | 156 (6.2) | <0.001 | 13 (13.7) | 59 (5.1) | <0.01 | 0 (0.0) | 15 (1.3) | 1.00[c] |
| Tracheostomy | 32 (7.6) | 120 (4.7) | 0.01 | 11 (11.6) | 34 (3.0) | <0.001 | 1 (11.1) | 111 (10.0) | 0.60[c] |
| Endotracheal tube | 72 (17.2) | 369 (14.5) | 0.16 | 17 (17.9) | 152 (13.2) | 0.20 | 0 (0.0) | 21 (1.8) | 1.00[c] |
| Nasogastric tube | 179 (42.7) | 724 (28.5) | <0.001 | 33 (34.7) | 248 (21.6) | <0.01 | 8 (88.9) | 428 (37.3) | <0.01[c] |
| Chest tube | 8 (1.9) | 63 (2.5) | 0.48 | 2 (2.1) | 11 (1.0) | 0.26[c] | 0 (0.0) | 3 (0.3) | 1.00[c] |
| PEG tube | 86 (20.5) | 271 (10.7) | <0.001 | 10 (10.5) | 72 (6.3) | 0.11 | 3 (33.3) | 71 (6.2) | 0.02[c] |
| Suprapubic catheter | 1 (0.2) | 15 (0.6) | 0.72[c] | 1 (1.1) | 4 (0.4) | 0.33[c] | 0 (0.0) | 17 (1.5) | 1.00[c] |
| Indwelling urinary catheter | 199 (47.5) | 809 (31.9) | <0.001 | 50 (52.6) | 397 (34.6) | <0.001 | 4 (44.4) | 179 (15.6) | 0.04[c] |
| Colostomy | 14 (3.3) | 30 (1.2) | <0.01 | 2 (2.1) | 11 (1.0) | 0.26[c] | 0 (0.0) | 10 (0.9) | 1.00[c] |
| Details of current and prior hospital admissions | | | | | | | | | |
| Median (IQR) length of stay (days) | 15 (9–30) | 9 (6–16) | <0.001[b] | 20 (10–36) | 22 (11–37) | 0.19[b] | 691 (139–2,407) | 503 (223–1,665) | 0.69[b] |
| No. (%) of subsidized patients | 404 (96.4) | 2,305 (90.9) | <0.001 | 86 (90.5) | 1,044 (90.9) | 0.91 | 9 (100.0) | 1,147 (99.9) | 1.00[c] |
| No. (%) of patients with prior ICU admission | 28 (6.7) | 88 (3.5) | <0.01 | 22 (23.2) | 143 (12.5) | <0.01 | 0 (0.0) | 28 (2.4) | 1.00[c] |
| No. (%) of patients with prior admission to ACH | | | | | | | | | |
| None | 157 (37.5) | 1,440 (56.8) | <0.001 | 2 (2.1) | 85 (7.4) | 0.08 | 1 (11.1) | 695 (60.5) | <0.01[c] |
| Study ACH | 262 (62.5) | 1,097 (43.2) | <0.001 | 46 (48.4) | 588 (51.2) | 0.08 | 6 (66.7) | 227 (19.8) | |
| Other ACHs | | | | 47 (49.5) | 476 (41.4) | | 2 (22.2) | 226 (19.7) | |
| No. of prior admissions to ACH | | | | | | | | | |
| Median (IQR) | 2 (1–4) | 1 (1–3) | <0.001[b] | 2 (1–3) | 1 (1–2) | <0.001[b] | 3 (2–4) | 1 (1–2) | <0.01[b] |
| Range | 1–20 | 1–25 | | 1–9 | 1–19 | | 1–8 | 1–10 | |
| No. (%) patients using the following medications: | | | | | | | | | |
| Antacid | 11 (2.6) | 67 (2.6) | 0.99 | 4 (4.2) | 55 (4.8) | 1.00[c] | 0 (0.0) | 17 (1.5) | 1.00[c] |
| Proton pump inhibitors | 364 (86.9) | 1,802 (71.0) | <0.001 | 77 (81.1) | 723 (62.9) | <0.001 | 7 (77.8) | 488 (42.5) | 0.04[c] |
| H2 antagonists | 74 (17.7) | 354 (14.0) | 0.05 | 6 (6.3) | 164 (14.3) | 0.03 | 4 (44.4) | 189 (16.5) | 0.05[c] |
| Corticosteroids | 94 (22.4) | 520 (20.5) | 0.37 | 23 (24.2) | 166 (14.5) | 0.01 | 3 (33.3) | 118 (10.3) | 0.06[c] |
| Aminoglycosides | 187 (44.6) | 784 (30.9) | <0.001 | 24 (25.3) | 139 (12.1) | <0.001 | 5 (55.6) | 114 (9.9) | <0.01[c] |
| Carbapenems | 140 (33.4) | 345 (13.6) | <0.001 | 28 (29.5) | 107 (9.3) | <0.001 | 1 (11.1) | 49 (4.3) | 0.33[c] |
| Cephalosporins | 199 (47.5) | 738 (29.1) | <0.001 | 49 (51.6) | 344 (29.9) | <0.001 | 4 (44.4) | 133 (11.6) | 0.02[c] |
| Fluoroquinolones | 139 (33.2) | 471 (18.6) | <0.001 | 43 (45.3) | 276 (24.0) | <0.001 | 7 (77.8) | 237 (20.6) | <0.001[c] |
| Penicillin | 367 (87.6) | 1,738 (68.5) | <0.001 | 80 (84.2) | 645 (56.1) | <0.001 | 9 (100.0) | 590 (51.4) | <0.01[c] |
| Vancomycin | 267 (63.7) | 771 (30.4) | <0.001 | 40 (42.1) | 170 (14.8) | <0.001 | 6 (66.7) | 96 (8.4) | <0.001[c] |
| No. (%) patients with the following no. of days of antibiotic therapy[a]: | | | | | | | | | |
| None | 11 (2.6) | 468 (18.4) | <0.001 | 3 (3.2) | 315 (27.4) | <0.001[c] | 0 (0.0) | 437 (38.1) | 0.06[c] |
| 1–3 | 18 (4.3) | 238 (9.4) | | 1 (1.0) | 84 (7.3) | | 0 (0.0) | 9 (0.8) | |
| 4–7 | 42 (10.0) | 428 (16.9) | | 5 (5.3) | 125 (10.9) | | 0 (0.0) | 89 (7.7) | |
| >7 | 348 (83.1) | 1,403 (55.3) | | 84 (88.4) | 595 (51.8) | | 9 (100.0) | 606 (52.8) | |
| Unknown | | | | 2 (2.1) | 30 (2.6) | | 0 (0.0) | 7 (0.6) | |
| Surgery, wounds, and ulcers | | | | | | | | | |
| No. (%) patients with surgery in the past: | | | | | | | | | |
| 30 days | 171 (40.8) | 854 (33.7) | <0.01 | 21 (22.1) | 262 (22.8) | 0.88 | 1 (11.1) | 19 (1.7) | 0.15[c] |
| 90 days | 218 (52.0) | 1,036 (40.8) | <0.001 | 60 (63.2) | 518 (45.1) | <0.01 | 2 (22.2) | 50 (4.4) | 0.06[c] |
| 180 days | 240 (57.3) | 1,140 (44.9) | <0.001 | 66 (69.5) | 600 (52.2) | <0.01 | 2 (22.2) | 91 (7.9) | 0.16[c] |
| 365 days | 252 (60.1) | 1,262 (49.7) | <0.001 | 68 (71.6) | 635 (55.3) | <0.01 | 2 (22.2) | 179 (15.6) | 0.64[c] |

(Continued on next page)

**TABLE 2** (Continued)

| Characteristic | Value(s) for patients in: | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ACH ($n$ = 2,956) | | | ITCFs ($n$ = 1,244) | | | LTCFs ($n$ = 1,157) | | |
| | VRE positive ($n$ = 419) | VRE negative ($n$ = 2,537) | $P_1$ | VRE positive ($n$ = 95) | VRE negative ($n$ = 1,149) | $P_2$ | VRE positive ($n$ = 9) | VRE negative ($n$ = 1,148) | $P_3$ |
| No. (%) patients with a wound | 259 (61.8) | 903 (35.6) | <0.001 | 65 (68.4) | 637 (55.4) | 0.01 | 7 (77.8) | 413 (36.0) | 0.01[c] |
| No. (%) patients with a skin ulcer | 169 (40.3) | 479 (18.9) | <0.001 | 37 (39.0) | 229 (19.9) | <0.001 | 5 (55.6) | 196 (17.1) | 0.01[c] |
| Prior carriage of antimicrobial-resistant organism | | | | | | | | | |
| VRE | 55 (13.1) | 39 (1.5) | <0.001 | 7 (7.4) | 13 (1.1) | <0.001[c] | 1 (11.1) | 29 (2.5) | 0.21[c] |
| CRE | 6 (1.4) | 30 (1.2) | 0.67 | 2 (2.1) | 5 (0.4) | 0.09[c] | 0 (0.0) | 2 (0.2) | 1.00[c] |
| MRSA | 180 (43.0) | 450 (17.7) | <0.001 | 29 (30.5) | 191 (16.6) | <0.01 | 5 (55.6) | 131 (11.4) | <0.01[c] |

[a]Days of antibiotic therapy included the use of any antibiotics comprising an aminoglycoside, a carbapenem, a cephalosporin, a fluoroquinolone, penicillin, or vancomycin in the preceding 12 months.
[b]Wilcoxon rank-sum test.
[c]Fisher's exact test.
[d]Abbreviations: ACH, acute-care hospital; CCI, Charlson's comorbidity index; CRE, carbapenem-resistant enterococci; ITCFs, intermediate-term care facilities; IQR, interquartile range; LTCFs, long-term care facilities; MRSA, methicillin-resistant *Staphylococcus aureus*; PEG, percutaneous endoscopic gastrostomy; VRE, vancomycin-resistant enterococci. $P_1$, statistical test between VRE-positive and -negative patients in acute-care hospital; $P_2$, statistical test between VRE-positive and -negative patients in intermediate-term care facilities; $P_3$, statistical test between VRE-positive and -negative patients in long-term care facilities.

prior VRE carriage, the duration of antibiotic therapy, surgery in the past 90 days, and the presence of a skin ulcer were common risk factors. Factors such as the number of beds per room, prior MRSA carriage, and length of stay had different effects in the ACH than in ITCFs. While an increase in the number of beds per room, prior PPI use, prior MRSA carriage, and a prolonged length of stay of >14 days at the ACH were associated with an increased risk for VRE colonization at the ACH, they were not found to be risk factors in ITCFs. Notably, a length of stay of >14 days in ITCFs was inversely associated with VRE colonization.

We found that PPI use was a significant risk factor for VRE colonization, a finding consistent with that of previous studies (29, 30). An animal study showed that suppression of gastric acid by PPI acted in combination with other factors that disrupt the colonic microflora to encourage VRE colonization (30). Other studies have shown that H2 antagonists, which also increase gastric pH, are not associated with VRE colonization (31), similar to our study's finding.

We further observed that the use of antibiotics of all classes predisposed both ACH- and ITCF-admitted patients to VRE colonization. This is consistent with previous reports suggesting that antibiotic pressure selected for vancomycin resistance in enterococci (32–34). This also highlights the importance of good antimicrobial stewardship not only in ACHs but also in ITCFs for the prevention of VRE.

The presence of skin ulcers doubled the risk of VRE colonization in patients from both the ACH and ITCFs. This is consistent with the findings of prior studies in ACHs (35) and ILTCFs (36) showing that ulcers are independently associated with a higher risk of VRE colonization. A prior study suggested further surveillance of VRE colonization in patients with decubitus ulcers due to the potential spread of vancomycin resistance genes to staphylococci (35).

Our study illustrated that the effect of the duration of hospitalization was modified by the type of health care facility at which the patient was hospitalized. A length of stay of >14 days was positively associated with colonization in the ACH but inversely associated with colonization in ITCFs. Benenson et al also reported that a shorter duration of stay was associated with a higher risk of VRE colonization in ILTCFs (37). Mody et al. have further observed that a prolonged hospitalization of >14 days at an ACH prior to admission to the ITCF (adjusted OR, 2.15; 95% CI, 1.11 to 4.16) was an independent predictor of colonization with multidrug-resistant organisms (MRSA, VRE, and resistant Gram-negative bacilli), even after adjusting for the duration of stay in the ITCF (23). These findings suggest that patients might have been colonized in ACHs before transfer to ITCFs. A recent study conducted in the United Kingdom used whole-genome sequencing to demonstrate that LTCF residents acquired VRE from the ACH in the health care network and could transmit existing strains to ACH patients and

**TABLE 3** Multivariable logistic regression analysis of epidemiologic and clinical risk factors for VRE colonization[b]

| Characteristic | Model 1 | | Model 2 | | Model 3 | | Model 4 (final model) | |
|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | *P* | OR (95% CI) | *P* | OR (95% CI) | *P* | OR (95% CI) | *P* |
| Demographics | | | | | | | | |
| Age (yr) | 1.00 (0.99–1.01) | 0.55 | 1.00 (1.00–1.01) | 0.32 | 1.00 (1.00–1.01) | 0.27 | 1.00 (1.00–1.01) | 0.24 |
| Male | 1.16 (0.94–1.42) | 0.16 | 1.15 (0.94–1.41) | 0.18 | 1.16 (0.94–1.42) | 0.16 | 1.16 (0.94–1.42) | 0.17 |
| Yr of screening | | | | | | | | |
| 2014 | Reference | | Reference | | Reference | | Reference | |
| 2015 | 0.79 (0.63–1.00) | 0.05 | 0.78 (0.62–0.98) | 0.03 | 0.77 (0.61–0.98) | 0.03 | 0.78 (0.62–0.98) | 0.04 |
| 2016 | 0.47 (0.37–0.61) | <0.001 | 0.45 (0.35–0.58) | <0.001 | 0.45 (0.35–0.57) | <0.001 | 0.45 (0.35–0.57) | <0.001 |
| Comorbidities and prior carriage of antimicrobial-resistant organism | | | | | | | | |
| CCI > 5 | 0.98 (0.78–1.22) | 0.83 | 0.91 (0.73–1.15) | 0.44 | 0.89 (0.71–1.13) | 0.35 | 0.89 (0.70–1.12) | 0.33 |
| Prior carriage of VRE | 5.86 (3.91–8.79) | <0.001 | 5.69 (3.77–8.59) | <0.001 | 5.32 (3.50–8.09) | <0.001 | 5.23 (3.43–7.97) | <0.001 |
| Prior carriage of MRSA | 2.00 (1.61–2.48) | <0.001 | 1.86 (1.49–2.33) | <0.001 | 1.85 (1.47–2.31) | <0.001 | 1.83 (1.46–2.29) | <0.001 |
| Details of current and prior hospital admissions | | | | | | | | |
| Admitted to health care facility | | | | | | | | |
| ACH | Reference | | Reference | | Reference | | Reference | |
| ITCFs | 0.50 (0.38–0.65) | <0.001 | 0.48 (0.37–0.63) | <0.001 | 0.49 (0.37–0.64) | <0.001 | 0.77 (0.48–1.24) | 0.28 |
| LTCFs | 0.04 (0.02–0.09) | <0.001 | 0.05 (0.03–0.11) | <0.001 | 0.06 (0.03–0.13) | <0.001 | 0.05 (0.02–0.13) | <0.001 |
| Length of stay of >14 days | 1.42 (1.14–1.76) | <0.01 | 1.32 (1.06–1.65) | 0.01 | 1.28 (1.02–1.60) | 0.03 | 0.61 (0.38–0.96) | 0.03 |
| Prior admission to study ACH | 1.08 (0.87–1.35) | 0.48 | 1.05 (0.84–1.31) | 0.66 | 1.00 (0.80–1.25) | 0.99 | 1.01 (0.80–1.26) | 0.96 |
| No. of beds per room | | | | | | | | |
| 1 | Reference | | Reference | | Reference | | Reference | |
| 2–4 | 1.43 (0.90–2.28) | 0.13 | 1.36 (0.85–2.18) | 0.20 | 1.36 (0.85–2.18) | 0.20 | 1.37 (0.86–2.20) | 0.19 |
| 5–8 | 1.57 (1.12–2.21) | <0.01 | 1.61 (1.14–2.26) | <0.01 | 1.61 (1.14–2.27) | <0.01 | 1.61 (1.14–2.27) | <0.01 |
| >8 | 1.99 (1.28–3.09) | <0.01 | 2.13 (1.37–3.33) | <0.01 | 2.14 (1.37–3.35) | <0.01 | 2.06 (1.32–3.23) | <0.01 |
| Proton pump inhibitor use | 1.79 (1.37–2.34) | <0.001 | 1.70 (1.29–2.22) | <0.001 | 1.63 (1.24–2.15) | <0.001 | 1.63 (1.24–2.14) | <0.01 |
| No. of days of antibiotic therapy[a] | | | | | | | | |
| 0 | Reference | | Reference | | Reference | | Reference | |
| 1–3 | 3.24 (1.59–6.58) | <0.01 | 3.04 (1.49–6.19) | <0.01 | 2.77 (1.36–5.65) | <0.01 | 2.79 (1.37–5.70) | <0.01 |
| 4–7 | 4.13 (2.24–7.62) | <0.001 | 4.00 (2.17–7.39) | <0.001 | 3.57 (1.92–6.63) | <0.001 | 3.59 (1.93–6.67) | <0.001 |
| >7 | 7.54 (4.34–13.09) | <0.001 | 6.54 (3.76–11.38) | <0.001 | 5.69 (3.24–9.98) | <0.001 | 5.62 (3.20–9.87) | <0.001 |
| Unknown | 4.10 (0.87–19.36) | 0.08 | 3.52 (0.74–16.84) | 0.12 | 3.10 (0.65–14.85) | 0.16 | 2.97 (0.62–14.15) | 0.17 |
| Surgery and ulcer | | | | | | | | |
| Surgery in the past 90 days | | | 1.59 (1.29–1.96) | <0.001 | 1.51 (1.23–1.87) | <0.001 | 1.44 (1.17–1.79) | <0.01 |
| Presence of a skin ulcer | | | 1.70 (1.37–2.11) | <0.001 | 1.68 (1.35–2.09) | <0.001 | 1.74 (1.40–2.17) | <0.001 |
| Indwelling devices | | | | | | | | |
| Peripheral line | | | | | 1.79 (0.94–3.43) | 0.08 | 1.69 (0.88–3.25) | 0.12 |
| Dialysis line | | | | | 1.29 (0.92–1.80) | 0.14 | 1.29 (0.92–1.81) | 0.14 |
| PEG tube | | | | | 0.93 (0.70–1.24) | 0.64 | 0.91 (0.68–1.21) | 0.52 |
| Indwelling urinary catheter | | | | | 1.24 (1.01–1.53) | 0.04 | 1.63 (1.04–2.56) | 0.03 |
| Interaction between ACH and: | | | | | | | | |
| Length of stay of >14 days | | | | | | | 2.61 (1.55–4.39) | <0.001 |
| Presence of an indwelling urinary catheter | | | | | | | 0.69 (0.42–1.14) | 0.15 |
| Model assessment | | | | | | | | |
| Log likelihood | −1,376.9879 | | −1,356.6193 | | −1,351.6096 | | −1,344.6439 | |
| Likelihood-ratio test *P* value | | | <0.001 | | 0.04 | | <0.01 | |
| Area under ROC | 0.8163 | | 0.8229 | | 0.8248 | | 0.8278 | |

[a]Days of antibiotic therapy included the use of any antibiotics comprising an aminoglycoside, a carbapenem, a cephalosporin, a fluoroquinolone, penicillin, or vancomycin in the preceding 12 months.

[b]Data are for 5,357 patients. Abbreviations: ACH, acute-care hospital; CCI, Charlson's comorbidity index; CI, confidence interval; ITCFs, intermediate-term care facilities; LTCFs, long-term care facilities; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; ROC, receiver operating curve; PEG, percutaneous endoscopic gastrostomy; VRE, vancomycin-resistant enterococci.

shed VRE into the environment (38). However, no evidence of VRE transmission between LTCF residents could be found. Further studies are needed to understand the transmission dynamics between ITCFs and the ACH in a health care network.

The number of beds per room was a significant risk factor for VRE colonization in the ACH. This finding was similar to that of previous studies (20, 39). This could be due to more frequent contact precaution lapses when faced with higher patient-to-staff ratios (40). However, this was not observed in ITCFs, where the care model differed from that

**TABLE 4** Multivariable logistic regression analysis of epidemiologic and clinical risk factors for VRE colonization in the ACH and ITCFs[b]

| Characteristic | ACH ($n$ = 2,956) | | ITCFs ($n$ = 1,244) | |
|---|---|---|---|---|
| | OR (95% CI) | $P$ | OR (95% CI) | $P$ |
| Demographics | | | | |
| Age (yr) | 1.01 (1.00–1.01) | 0.19 | 1.00 (0.98–1.02) | 0.82 |
| Male | 1.10 (0.87–1.39) | 0.44 | 1.53 (0.96–2.46) | 0.08 |
| Yr of screening | | | | |
| 2014 | Reference | | Reference | |
| 2015 | 0.64 (0.49–0.83) | <0.01 | 1.73 (0.94–3.19) | 0.08 |
| 2016 | 0.35 (0.26–0.47) | <0.001 | 1.27 (0.66–2.43) | 0.47 |
| Comorbidities and prior carriage of antimicrobial-resistant organism | | | | |
| CCI > 5 | 0.89 (0.69–1.16) | 0.39 | 0.82 (0.42–1.59) | 0.56 |
| Prior carriage of VRE | 6.29 (3.86–10.25) | <0.001 | 3.45 (1.16–10.28) | 0.03 |
| Prior carriage of MRSA | 1.87 (1.44–2.43) | <0.001 | 1.47 (0.88–2.45) | 0.14 |
| Details of current and prior hospital admissions | | | | |
| Length of stay >14 days | 1.71 (1.32–2.21) | <0.001 | 0.51 (0.32–0.84) | <0.01 |
| Prior admission to ACH | | | | |
| None | Reference | | Reference | |
| Study ACH | 1.15 (0.89–1.51) | 0.29 | 1.73 (0.37–8.02) | 0.49 |
| Other ACHs | – | | 2.52 (0.54–11.78) | 0.24 |
| No. of beds per room | | | | |
| 1 | Reference | | Reference | |
| 2–4 | 1.54 (0.94–2.53) | 0.09 | 0.27 (0.04–1.67) | 0.16 |
| 5–8 | 1.79 (1.24–2.57) | <0.01 | 0.29 (0.07–1.14) | 0.08 |
| >8 | 2.12 (1.24–3.62) | <0.01 | 0.42 (0.10–1.73) | 0.23 |
| Medication use | | | | |
| Proton pump inhibitors | 1.61 (1.16–2.22) | <0.01 | 1.73 (0.98–3.08) | 0.06 |
| No. of days of antibiotic therapy[a] | | | | |
| 0 | Reference | | Reference | |
| 1–3 | 2.93 (1.34–6.41) | <0.01 | 0.81 (0.08–8.10) | 0.86 |
| 4–7 | 3.35 (1.67–6.71) | <0.01 | 3.45 (0.79–15.04) | 0.10 |
| >7 | 4.44 (2.32–8.51) | <0.001 | 7.80 (2.35–25.87) | <0.01 |
| Unknown | | | 3.61 (0.55–23.57) | 0.18 |
| Surgery and ulcer | | | | |
| Surgery in the past 90 days | 1.45 (1.14–1.85) | <0.01 | 1.62 (1.00–2.62) | 0.05 |
| Presence of a skin ulcer | 1.65 (1.27–2.13) | <0.001 | 1.99 (1.22–3.24) | <0.01 |
| Indwelling devices | | | | |
| Peripheral line | 1.43 (0.60–3.38) | 0.42 | 1.26 (0.45–3.49) | 0.66 |
| Dialysis line | 1.24 (0.84–1.83) | 0.27 | 1.36 (0.65–2.87) | 0.41 |
| PEG tube | 0.86 (0.62–1.18) | 0.35 | 1.28 (0.58–2.82) | 0.54 |
| Indwelling urinary catheter | 1.15 (0.91–1.47) | 0.25 | 1.54 (0.94–2.51) | 0.08 |

[a]Days of antibiotic therapy included the use of any antibiotics comprising an aminoglycoside, a carbapenem, a cephalosporin, a fluoroquinolone, penicillin, or vancomycin in the preceding 12 months.

[b]Abbreviations: ACH, acute-care hospital; CCI, Charlson's comorbidity index; CI, confidence interval; ITCFs, intermediate-term care facilities; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; PEG, percutaneous endoscopic gastrostomy; VRE, vancomycin-resistant enterococci.

in the ACH. Whether patients were hospitalized in single- or multibed rooms in ITCFs, they would be exposed to the common gym facilities during their physical and occupational therapies for rehabilitation.

The use of indwelling urinary catheters increased the risk of VRE colonization in ITCFs with marginal statistical significance (OR, 1.54; 95% CI, 0.94 to 2.51; $P = 0.08$) but had no influence on VRE colonization in the ACH (OR, 1.15; 95% CI, 0.91 to 1.47; $P = 0.25$). This could be due to the longer duration of catheter use in ITCF-admitted patients, whose conditions might require long-term catheter use. McKinnell et al. have also reported an increased risk of VRE colonization in long-stay nursing home residents who had a urinary catheter (adjusted OR, 2.7; 95% CI, 1.5 to 5.1) (28). Indwelling urinary catheters are well-known sources of colonization and infection (41), and VRE are a common cause of urinary tract infections (26, 42). Another reason could be the

know-do gap between the knowledge of best practices and the actual implementation of the evidence-based catheterization techniques in ILTCFs, a well-studied discrepancy (43, 44). Suboptimal practices predispose patients to VRE colonization (45), highlighting the importance of staff education and training on catheter management to reduce colonization risk (46).

Prior VRE carriers were 6 and 3.5 times as likely as noncarriers to be currently colonized with VRE in the ACH and ITCFs, respectively. This observation supports the strategy of preemptive isolation or cohorting with contact precautions for prior VRE carriers on admission to ACHs and ITCFs.

There was no significant relationship between comorbidities and the risk of colonization after accounting for extrinsic factors. Amenable extrinsic factors, such as exposure to antibiotics and a prolonged stay of >14 days at the ACH, were significantly associated with VRE colonization. This is corroborated by several studies examining VRE colonization in dialysis centers, where invasive devices and prolonged exposure to health care settings rather than the patients' comorbidities were suggested to be risk factors (47, 48).

The strength of this study is that it included a large sample of patients and a high participation rate (87%). Hence, selection bias, if any, was likely minimal. VRE screening samples and tests were collected and performed in a standardized manner, with the identification of bacterial colonies being confirmed with matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry, minimizing any potential measurement error and outcome misclassification. A limitation of the study was the unavailability of data on previous hospitalization in ACHs other than the study's ACH for the ACH-admitted population. However, any information bias was likely nondifferential and minimal, as the majority of patients from the study's ACH tended to be readmitted to the same ACH. Another limitation was that health care system-specific risk factors in the Singapore population, particularly under the provision of subsidized care, may not be generalizable to other health care systems.

In conclusion, we identified similarities and differences in risk factors for VRE colonization in an ACH and its affiliated ITCFs. Prior VRE carriage, exposure to antibiotics, and the presence of a skin ulcer were risk factors common to the facilities. While the increasing number of beds per room increased the colonization risk in the ACH, it was not observed in ITCFs. A length of stay of >14 days was positively associated with VRE colonization in the ACH but inversely associated with colonization in ITCFs. Infection prevention and control strategies, including preemptive contact precautions and targeted screening, could be implemented for the respective high-risk patient groups at ACHs and ITCFs.

## MATERIALS AND METHODS

**Study setting and design.** Over three 6-week periods from 2 June to July 9 2014, 22 June to 31 July 2015, and 30 June to 29 July 2016, serial cross-sectional studies were conducted in a 1,700-bed adult tertiary-care ACH in Singapore and its three most closely affiliated ITCFs, a 100-bed rehabilitation hospital, a 116-bed community hospital, and a 235-bed community hospital which expanded to 360 beds in 2015, as well as its three affiliated LTCFs, a 234-bed nursing home, a 164-bed chronic sick unit, and a 236-bed nursing home newly opened in 2015. In the ITCFs and LTCFs, no VRE screening protocol was in place throughout the study period. In the ACH, targeted on-admission VRE screening had been carried out since January 2014 for patients who had either chronic renal disease or a prior hospitalization in the preceding 12 months. Patients identified to be colonized with VRE were placed in VRE cohort wards, with enhanced contact precautions being undertaken.

We randomly selected 2,956 inpatients with a >48-h stay in the ACH during the study period to participate in the study. A random sample of 65 to 66 eligible inpatients per day, proportional to the bed census of the ward, covering all wards in the ACH was selected systematically thrice over 15 days. All residents of the ITCFs and LTCFs were included.

**Sample collection and testing.** A rectal swab sample was taken from each study participant in a standardized manner, with a saline-moistened sterile swab stick being inserted 2 inches into the rectum, twirled twice, and removed. A stool sample was taken from participants who declined rectal swab samples collection. The samples were inoculated onto ChromID VRE-selective chromogenic agar and incubated aerobically at 35 to 37°C for 48 h. Positive cultures were referred to matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry and Vitek antimicrobial suscepti-

bility testing (AST) for identification. Isolates were genotyped via PCR, using previously identified methods (49).

**Epidemiologic and clinical data.** The patients' epidemiologic and clinical data collected included sociodemographics (age, gender, and ethnicity); comorbidity (diabetes mellitus, cardiovascular disease, liver disease, renal disease, neoplasm, central nervous system disease, and chronic pulmonary disease); cognitive function; prior VRE colonization in the 12 months preceding VRE screening; prior hospitalization at the acute-care hospital in the health care network or other acute-care hospitals in the preceding 12 months; a history of surgical procedures in the preceding 12 months; the number of beds per room during the current hospital stay, which was categorized into 1, 2 to 4, 5 to 8, and >8 beds per room; the presence of a wound and/or a skin ulcer and percutaneous invasive devices in the preceding 12 months; the length of stay at the institution at the time of screening; and prior antibiotic, proton pump inhibitor (PPI), H2 antagonist, and corticosteroid exposures by any route of administration with ≥1 day of therapy (DOT) (50) in the preceding 12 months. Prior antibiotic exposure was further categorized into 0, 1 to 3, 4 to 7, and >7 DOT. Charlson's comorbidity index (CCI) (51) was computed from the presence of comorbidities and categorized into ≤5 (good) and >5 (poor premorbid status).

Data were obtained electronically from the admission and discharge databases of all institutions and electronically from medical and pharmacy records at the ACH and ILTCFs. In the ILTCFs, where electronic records were unavailable, clinical data were manually extracted from paper-based inpatient medical records by trained research assistants.

**Data analysis.** We used frequencies and percentages for categorical variables and medians and interquartile ranges (IQR) for continuous variables for descriptive analyses. The differences in characteristics between VRE-colonized and noncolonized patients were compared using the chi-square test or Fisher's exact test where appropriate. Differences in age and the duration of stay were compared using the Wilcoxon rank-sum test, as the data did not follow a normal distribution. We explored the relationships between the various patients' characteristics and colonization with VRE using multivariable logistic regression models, adjusting for potential confounders. Four nested multivariable logistic regression models were constructed, with VRE colonization being the outcome variable and the following variables being predictors: in model 1, demographics and comorbidities; current and prior hospital admission details, including length of stay and the number of beds per room; and antibiotic and PPI exposures; in model 2, addition of skin ulcers and surgery in the preceding 90 days; in model 3, addition of indwelling invasive devices; and in model 4, final addition of interaction terms between ACH and length of stay/indwelling catheter use. The models were compared against each other using the likelihood-ratio test and receiver operating curve (ROC) values, and the best-fit model was chosen as the final model. The odds ratio (OR) with the 95% confidence interval (CI) from regression analyses is presented, along with *P* values. All reported *P* values were two-tailed with an $\alpha$ level of 0.05. All statistical analyses were performed using Stata (version 13.1) software (StataCorp LP, College Station, TX).

**Ethical approval.** Ethical approval for the study was obtained from the Domain Specific Research Board, National Healthcare Group (DSRB-2014/01139). Informed consent was provided by all cognitively intact participants or the legally authorized representatives (LARs) of cognitively impaired participants. A waiver of informed consent was granted for cognitively impaired participants from the ILTCFs who had no LARs.

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